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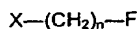
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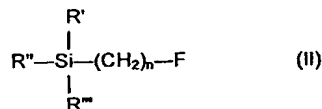
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(54) Title: PROCESS FOR THE PREPARATION OF FLUOROHALOALKANES



(I)



(II)

XY

(III)

(57) Abstract: The invention provides a process for preparation of a fluorohaloalkane, preferably an [<sup>18</sup>F]fluorohaloalkane of formula (I) wherein X is halo and n is an integer of from 1 to 6; which comprises: reaction of the corresponding organosilicon compound of formula (II); wherein n is as defined for the compound of formula (I); and R', R'', and R''' are independently selected from C<sub>1-6</sub> alkyl and C<sub>1-6</sub> haloalkyl; and R''' may alternatively be the group, with a compound of formula (III), wherein X is as defined for the compound of formula (I) and Y is halo. Intermediates having use in such processes are also claimed.

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# INTERNATIONAL SEARCH REPORT

International Application No  
PCT/GB 03/04026

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC 7 C07B59/00 C07C17/093 C07B39/00 C07F7/08				
According to International Patent Classification (IPC) or to both national classification and IPC				
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) IPC 7 C07B C07C C07F				
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched				
Electronic data base consulted during the International search (name of data base and, where practical, search terms used) EPO-Internal, BEILSTEIN Data, CHEM ABS Data, PAJ				
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>				
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
A	ZHANG M-R ET AL: "Development of an automated system for synthesizing F-labeled compounds using [F]fluoroethyl bromide as a synthetic precursor" APPLIED RADIATION AND ISOTOPES, PERGAMON PRESS LTD., EXETER, GB, vol. 57, no. 3, September 2002 (2002-09), pages 335-342, XP004370242 ISSN: 0969-8043 cited in the application example 3.1.1 ----- -/--	1,8,9		
<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.				
<input checked="" type="checkbox"/> Patent family members are listed in annex.				
<b>* Special categories of cited documents:</b>				
<table border="0"> <tr> <td style="vertical-align: top;">           "A" document defining the general state of the art which is not considered to be of particular relevance            "E" earlier document but published on or after the international filing date            "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)            "O" document referring to an oral disclosure, use, exhibition or other means            "P" document published prior to the international filing date but later than the priority date claimed         </td> <td style="vertical-align: top;">           "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention            "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone            "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.            "&amp;" document member of the same patent family         </td> </tr> </table>			"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family
"A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family			
Date of the actual completion of the international search 24 March 2004		Date of mailing of the international search report 26 03. 2004		
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 551 epo nl, Fax: (+31-70) 340-3016		Authorized officer Diederens, J		

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/04026

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	E.S. ALEXANDER ET AL.: "Polyfluoroalkyl Compounds of Silicon. Part IX. Silanes containing the Bis(trifluoromethyl)amino-group" J. CHEM. SOC. A, 1970, pages 2285-91, XP002266201 page 2887, product VIII right hand column, Me <sub>3</sub> SiCH <sub>2</sub> F -----	8
X	DIETMAR SEYFERTH ET AL.: "Halomethyl-metal compounds. Phenyl(fluorodibromomethyl)mercury, a fluorobromocarbene precursor" J. ORGANOMET. CHEM., vol. 51, 1973, pages 77-87, XP002266202 page 80, equation (4) Et <sub>3</sub> SiCH <sub>2</sub> F -----	8
X	EDMUND K.S. LIU ET AL.: "Fluorination of dimethylmercury, tetramethylsilane and tetramethylgermanium" J. ORGANOMET. CHEM., 1978, pages 167-82, XP002266203 page 171, Table 3, Si(CH <sub>3</sub> )(CH <sub>2</sub> F) <sub>2</sub> (CHF <sub>2</sub> ) -----	8
X	ROGER L. SCHOLL ET AL.: "Silicon-29 Chemical Shifts of Organosilicon Compounds" J. AM. CHEM. SOC., vol. 94, no. 18, 1972, pages 6376-85, XP002266204 page 78, Table 1, entry 4, (CH <sub>2</sub> F)(CH <sub>3</sub> ) <sub>2</sub> Si(n-C <sub>4</sub> H <sub>9</sub> ) -----	8
X	D. COOPER ET AL.: "Polyfluoroalkyl Compounds of Silicon. VIII Reactions of Silanes with Vinyl Fluoride and with 1-Chloro-2-fluoroethylene" J. CHEM. SOC. A, vol. 196, 1967, pages 2098-2103, XP002266205 page 2101 right hand column, 2nd paragraph, Me <sub>3</sub> SiCH <sub>2</sub> F -----	8
X	J. VCELAK ET AL.: "The exchange of fluorine in (gamma-fluoropropyl)trialkylsilanes and n-heptyl fluoride for halogens of grignard reagents" COLLECTION CZECHOSLOV. CHEM. COMMUN., vol. 41, 1976, pages 131-9, XP0008028871 EXPERIMENTAL: Synthesis of (gamma-fluoropropyl)triethylsilane from (gamma-chloropropyl)triethylsilane by reaction with KF ----- -/--	7

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 03/04026

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	J. VCELAK ET AL.: "19F-NMR spectra of (Fluoroalkyl)-Substituted Silanes" COLLECTION CZECHOSLOV. CHEM. COMMUN., vol. 41, 1976, pages 386-390, XP0008028870 EXPERIMENTAL. a) Synthesis of (Fluoromethyl)trimethylsilane from the corresponding tosylate and KF b) (epsilon-fluoropentyl)trimethylsilane from the corresponding alcohol and Yarovenko reagent -----	7
X	V.B. PUCHNAREVIC ET AL.: "Synthesis of gamma-fluoropropyl Substituted Silanes" COLLECTION CZECHOSLOV. CHEM. COMMUN., vol. 39, 1974, pages 2616-2620, XP0008028872 EXPERIMENTAL: Synthesis of (gamma-fluoropropyl)trimethylsilane by reaction of the alcohol and Yarovenko reagent, see page 2619 -----	7
X	JP 02 290885 A (SHIN ETSU CHEM CO. LTD) 30 November 1990 (1990-11-30) abstract -----	7

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# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/GB 03/04026

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 8  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a):

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 8

The initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claim(s) may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, it appears impossible to execute a meaningful search and to issue a complete search report over the whole breadth of claim 8. In the description there are no examples for compounds of claim 8, and there are no preferred embodiments within the description which could act as "fallback". Therefore, it is impossible to search claim 8 and to issue a complete search report over the whole breadth of this claim..

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-6 8,9

Process for the preparation of a fluorohaloalkane of Formula (I) and (Ia) by reaction of compound (II) (or IIa) with III, compounds of formula (II) and (IIa)

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2. claims: 7,10

Process for the preparation of compounds of Formula (II) or (IIa) by reaction of compound (IV) with a source of F-

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**Information on patent family members**

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